Specialty Conference

The Artificial Heart—Progress, Problems, Prognosis

Discussant
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This discussion was selected from the weekly Grand Rounds in the Department of Medicine, University of Washington School of Medicine, Seattle. Taken from a transcription, it has been edited by Drs Paul G. Ramsey, Associate Professor of Medicine, and Philip J. Fialkow, Professor and Chair of the Department of Medicine.

ROBERT L. VAN CITTERS, MD:* Heart disease is responsible for about 50% of all deaths in the United States. About a third of these deaths occur before the age of 65, some before age 35. Many of these early deaths occur in people without coexisting disease. The concept of an artificial heart arose from the belief that many early deaths could be postponed and the useful period of many lives extended if it were possible to replace the diseased heart with a prosthetic device.

Work had been under way toward developing such a device in a few laboratories as far back as the 1930s, but congressional identification of mechanical circulatory support as a priority area within the National Institutes of Health (NIH) in 1963 provided impetus for the subsequent development of the Artificial Heart Program of the National Heart, Lung and Blood Institute. Studies at that time projected that as many as 130,000 people annually might benefit from an artificial heart and that it was reasonable to anticipate the development of a device with acceptable operating characteristics within five years. More than 20 years and $200 million later, very substantial progress has been made toward that goal, but it will be at least five more years before a totally implantable device is available for clinical use.

Recent clinical trials in the private sector using a tethered, pneumatically actuated device have focused substantial controversy not only on that effort, but also on the Artificial Heart Program of the NIH and on the concept itself. It will be the purpose of this presentation to review some aspects of the historical development of the Artificial Heart Program of the NIH, to present a nontechnical description of its current status and to examine some of the questions that potential availability of an artificial heart has raised.

The concept of replacing natural organs with mechanical prostheses or of supplementing their function with assist devices was known and practiced in antiquity. Greek sculptures dating back to the fourth century BC depict persons with prosthetic limbs; 15th-century woodcuts show monks wearing spectacles as they peruse ancient manuscripts, and many well-known figures throughout history are known to have used dental prostheses. These and other early prosthetic devices shared several characteristics; all were external, inert, nonpowered and would in today's parlance be classified as "low-tech" devices. Further, their evolution was slow: wooden legs changed very little over many centuries, 15th-century spectacles differ only in style from those in use today and false teeth are still just that.

A fundamental change took place following World War II. Rapid advances in technology, the development of new biomaterials and an enhanced understanding of basic biologic processes led to the development and widespread use of a broad variety of new devices—lens implants, artificial joints, prosthetic vessels and valves. New technologies such as renal dialysis provided an assist for organ functions and advances in immunology, and newly developed surgical techniques led to the establishment of successful programs for cornea, kidney, heart and marrow transplantation.

Committing a serious effort to replace the heart with a mechanical device has been a relatively recent development. Several factors have contributed. A large share of our current knowledge of the function and control of the circulation has emerged recently. Important advances have been made also in the understanding of basic biologic processes, such as clotting mechanisms, and there has been a substantial enhancement in technical capability, such as the development of new materials and the application of electronics.

Despite deep-seated philosophic, religious and emotional connotations, the heart is, for practical purposes, primarily a pump—an organ whose fundamental function is a mechanical one. Technology today has a far greater capacity to replace body structures and functions that are mechanical than those

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ABBREVIATIONS USED IN TEXT
LVAD = left ventricular-assist device
NIH = National Institutes of Health

that are biochemical or neurohumoral. It is now technically possible to build excellent mechanical pumps, and the heart is a suitable candidate for replacement by a prosthetic device.

Historical Highlights in Artificial Heart Development

The first account in which experimental attempts were made to replace the heart's function in animals with a mechanical device was published by Gallois in 1812.[1] Gallois theorized,

> If one could substitute for the heart a kind of injection—of arterial blood, either natural or artificially made—one would succeed easily in maintaining alive indefinitely any part of the body whatsoever.

Over the next century several investigators reported intermittent progress toward developing techniques and apparatuses for perfusing organs.[2] The modern era of mechanical circulatory devices began, however, with the work of Gibbon and others on extracorporeal circulation in the 1930s, culminating in 1939 with Gibbon's seminal contribution of a heart-lung pump with a practical oxygenator.[3] Much of this work came to a standstill during World War II, but in the immediate postwar period the development of cardiac catheterization greatly enhanced the ability of physicians to diagnose congenital and valvular heart diseases and to plan new approaches for their management. Other advances, such as improvements in anesthesia, helped to broaden the range of cardiac conditions amenable to surgical treatment and provided impetus for further refinement of heart-lung pumps. In 1952 a mechanical device was first used to bypass the function of the left ventricle in a human patient during repair of a mitral valve,[4] and later in the same year the heart was totally bypassed with the use of a mechanical heart-lung pump during repair of an atrial-septal defect.[5] Thus, by 1952 mechanical replacement of the heart had taken place.

During the next decade several improvements were made and many new heart-lung pumps evolved. As replacements for the heart, however, all such devices had serious limitations; because of their great size they were necessarily external, and it soon became apparent that there was an inverse relationship between pump time and survival. Nevertheless, the development of these heart-lung pumps for use in the surgery set the stage for the development of an entirely implantable artificial heart.

In 1963 Congress appropriated $581,000 to the National Institutes of Health for the specific purpose of developing an artificial heart. At least in part, this targeted approach seems to have stemmed from the success of several other government agencies in directing high-priority research projects, such as the Manhattan Project or the space program. The Artificial Heart Program that emerged was among the first congressionally mandated programs at NIH and was, in turn, the National Heart Institute's first targeted research effort. A systems approach was adopted. The potential need for such a device was analyzed, estimates were made of its costs and benefits and a plan was adopted that called for an orderly approach to major technical programs and for development of a family of devices—emergency devices, temporary devices, short- and long-term assist devices and total replacement devices. To take advantage of expertise in industry, the standard NIH approach of investigator-initiated research was supplemented by research contracts with individual researchers, universities and commercial organizations. During the next several years, progress was made in developing instrumentation, evaluating the biocompatibility of materials and designing and testing components and prototypes. The initial goal of a completely implantable mechanical replacement by 1970, however, proved to be unrealistic.

Consequently, the focus of the program was shifted from a completely artificial heart to the staged development of a family of devices with the intermediate aim of developing a left ventricular-assist device (LVAD)—that is, a completely implanted pump with a single pumping chamber that could assist a failing ventricle by pumping blood from the left ventricle into the aorta. Work on a nuclear power source was terminated, and pneumatically activated devices were not pursued because these required tethering the patient to a large external console by tubes that passed through the chest wall to transmit power. Emphasis was placed on electrical and thermal engines. Strategies were implemented for an orderly sequence of bench and animal testing so that mechanical performance and physiologic effects could be validated in the long term before clinical investigation was initiated.

It has been the intent of the Artificial Heart Program to establish completely the efficacy of the LVAD as a preliminary step to proceeding with work on a totally implantable cardiac replacement system. This reflects decisions made early in the program that the assist device have fewer components and fewer sources of failure, that technologic problems are avoided by matching the performance of two pumps, that solutions to problems for the assist device can be applied to the total cardiac replacement system and that failure of the device would not result in immediate death. The immediate goal is to develop an electrically powered, fully implantable assist device with a two-year reliability (Figure 1). An electrical pump would remove blood from the left ventricle and return it to the descending aorta. The primary energy source is a rechargeable external battery pack, shown in Figure 1, to be worn as a belt. This set of batteries would require charging from a standard wall current every eight to ten hours. In addition, energy would be transmitted via electromagnetic coupling from an external coil, worn like a belt, to an implanted secondary coil connected to a small, implanted, rechargeable battery. This would provide power for 30 to 45 minutes of pump operation, during which time the patient could be free of any external connections. Implanted components of these assist devices weigh about 1,200 grams and occupy about 1,000 cc; the external battery pack weighs about 3,000 grams. Currently four completely implantable, electrically powered, left ventricular-assist systems are undergoing reliability tests on the bench and in animals. The immediate goal is to establish that a totally implantable assist system will meet a rigorous set of performance criteria defined in the device-readiness test program with two-year reliability.[6] The major performance criteria are listed in Table 1. It is anticipated that these tests will be completed in 1986 and one or more of these devices will become available for clinical

investigative use in 1987. A more distant goal is to create a device that would permit five years of reliable operation.

Development of an implantable, total heart replacement will follow the sequence established for assist devices—that is, validation through bench and animal testing, followed by clinical evaluation. As shown in Figure 2, the implanted, fully artificial heart would replace a diseased heart—that is, the natural heart would be removed and the inflow-outflow channels of the implanted device would connect with anatomically appropriate vessels. The entire heart is about 50% larger and heavier than the assist device. A thermal power system is currently under development that offers a potential for smaller size and weight and longer operation.

Why an Artificial Heart?

The rationale for developing an artificial heart relates to the perceived need. Subsequent study groups, however, have revised downward the estimate of 130,000 patients who might benefit each year from such a device. Estimates of the need must take into account such factors as subsequent medical and surgical progress, the effectiveness of new therapies, the decline in coronary heart disease and the recent awareness of prevention. They will differ from estimates of demand and will involve factors such as effectiveness of the device, quality of life and cost. For these reasons, and because clinical criteria have not yet been defined, it is not possible to come up with precise numerical estimates of actual usage.

A population-based study, however, was recently used to estimate the order of magnitude of the number of eligible candidates (D.G. Pesche, R.L. Frye, D.C. McGoon, et al: "Selection Criteria and Estimated Number of Candidates for the Total Artificial Heart in the Population of Olmsted County, Minnesota," unpublished data, May 1984). Charts of all patients within a defined population who had died during a five-year period were examined by a panel that used a precisely defined set of criteria to assess whether each patient might have been considered a candidate for management with an artificial heart. Only those patients between ages 15 and 69 years who had severe, irreversible depression of left ventric-

TABLE 1.—*Summary of Performance Goals Defined by Device Readiness Program for Current Generation of Left Ventricular Assist Systems*

Goal	*Unit*
Cardiac output	up to 10 liters/min
Heart rate	120/min
Blood pressure, systolic	120 mm of mercury
Filling pressure	0-15 mm of mercury
Simple control system	
At least 2 years reliable implanted operation	
No hemolysis, clot, emboli	
Compatible with body (nontoxic, noncorrosible and so forth)	
Impervious to body fluids, no leakage	
Operates at body temperature	
Rechargeable external energy supply	10 hours
Rechargeable internal energy supply	30 min
Operates in any orientation or environment	
Shape, weight, volume compatible with anatomy	
Psychologically acceptable level of noise, vibration and so forth	

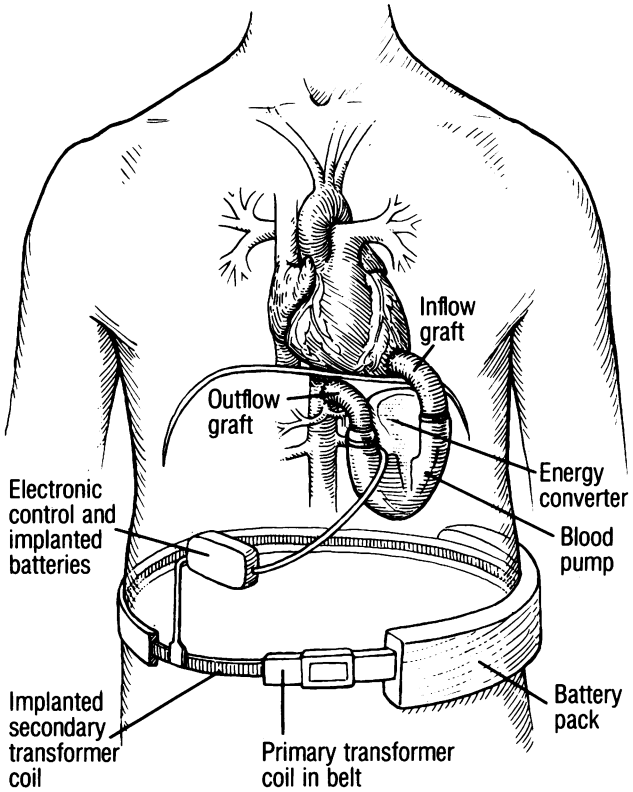

Figure 1.—The diagram shows a fully implantable, left ventricular-assist system (reproduced by permission of Devices and Technology Branch, National Heart, Lung and Blood Institute, National Institutes of Health).

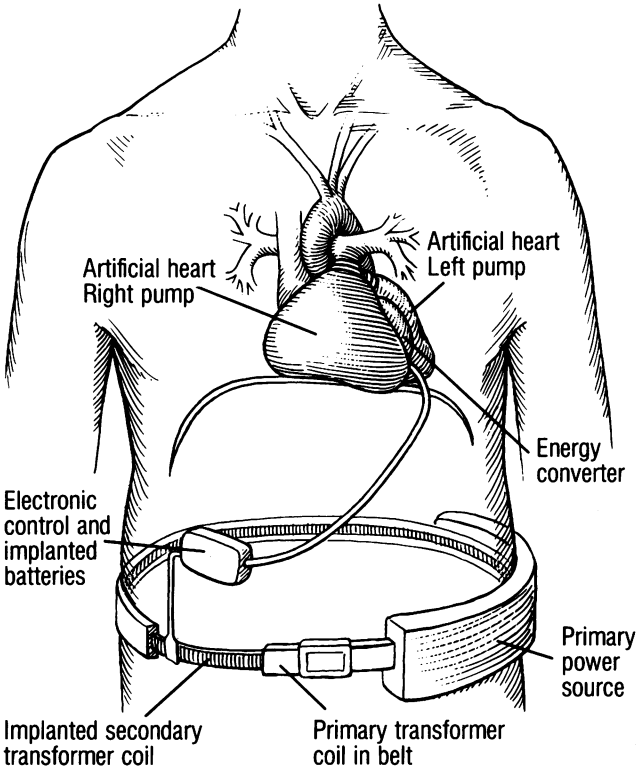

Figure 2.—The diagram shows a fully implantable, electrically actuated, completely artificial heart system (reproduced by permission of Devices and Technology Branch, National Heart, Lung and Blood Institute, National Institutes of Health).

ular function, were free of other coexisting disease and arrived at hospital at least two hours before death were considered to be potential candidates. Only about 14% of all patients who died of cardiac disease between ages 15 and 69 years (or 1.5% of all deaths in that age group) met those criteria. When these data were extrapolated to the US population to establish an order of magnitude, the potential number of candidates was in the range of 17,000 to 35,000. The major exclusion criteria were sudden death and coexisting disease. The average age of the potential recipients was 59 years, nearly 80% were male and the cause of ventricular failure in more than 50% was coronary artery disease.

The actual numbers will be influenced by the extent to which the device is accepted by society. The primary factor affecting societal acceptance is likely to be the performance record of the device—that is, does it work? In the case of other innovations, such as cardiac pacemakers or prosthetic valves and vessels, the fact that the devices were capable of carrying out their intended function in a very high percentage of cases contributed to both broadened public acceptance and expanded medical indications. Even without proof of efficacy, however, the specter of impending death is a powerful motivator for accepting heroic measures. For example, more than 200,000 coronary artery bypass graft procedures were done before effectiveness of the operation was scientifically evaluated, and even now a relatively small fraction of the 200,000 patients on whom the operation is carried out each year fit rigorously defined criteria. In our technologically oriented society, the public has come to accept, expect and even demand access to new medical procedures and devices. There is little reason to expect any difference in the case of the artificial heart; if the device is available, it will be used.

Issues related to cost—both to the individual patient and to society—will also play a role in determining the demand for the artificial heart. In 1963, at the time the artificial heart program was started, the cost of the device was estimated to be about $5,000. In the intervening years, five study groups have projected successively higher cost estimates.[7-11] The most recent study estimated that the cost of the device, its implantation and subsequent medical follow-up will be $150,000 (in 1983 dollars).[12] More than $100,000 of these costs are associated with hospital and medical care. Artificial Heart Program officials estimate that production costs for the device itself will initially be in the range of $40,000, but that this figure might be reduced to as low as $10,000 by economies of scale if the device were put into production. If one applies the $150,000 unit cost to the estimated range of possible recipients—17,000 to 35,000—then the cost to society might range between $2.5 and $5 billion per year. Some sense of the scale and proportion of these costs may be gained from comparison with society's costs for other procedures: cardiac pacemakers incur costs of $2 billion, the renal dialysis and renal transplant programs jointly cost more than $3 billion; the cost of a heart transplant is in the $60,000 to $120,000 range and liver transplants exceed $150,000. Thus, the projected cost for an artificial heart is likely to be in the same general range as many other expensive but accepted procedures and comparable to a number of medically acceptable procedures with unproved efficacy.

Pauker, a member of the Working Group on Mechanical Circulatory Support, has used modeling techniques to compare the costs and prognoses of patients treated with conventional medical therapy with those treated with an artificial heart.[12] In brief, using a model, a cohort of class IV cardiac patients were tracked through both courses of therapy over a defined period of time and the range of costs computed when a defined set of assumptions such as diagnostic procedures, hospital care, surgery and major and minor complications were entered into the model. In this study, class IV cardiac patients managed medically could be expected to survive for an average of less than six months and generate average medical costs of about $20,000, whereas identical patients treated with an artificial heart would be expected to survive 54 months at a cost of $150,000. That is, 48 months of additional survival might be "bought" at a cost of about $30,000 per year.

Quality of life must necessarily be a consideration in evaluating any medical procedure. It is a fact that the quality of life is compromised following many heroic procedures. Until actual experience has accumulated through controlled clinical trials, there is no way to predict with certainty what the quality of life will be for patients with an artificial heart. Even if the goal of an extended span of life is achieved and with a reasonable range of ambulation and activities, patients will not be able to forget they have the device. There will be individual adjustments to cues to the presence of the device such as noise, weight or vibration, to housekeeping requirements such as battery changes or anticoagulants or to the risks of more serious complications or the threat of device failure. The nature of the undertaking—permanent replacement of a vital organ—implies a trade-off between risk and benefit. Complications, both minor and catastrophic, are inevitable, and there will be a learning curve.

Ethical Issues

Medical economists have observed that dissemination of a new medical technology proceeds in the manner of a ratchet. That is, once accepted, the range of conditions or medical indications for a new device or technology tends to creep, and public acceptance, or even demand, makes the process irreversible. While the artificial heart is far from an accepted therapy, evidence has already accumulated that this phenomenon is likely to prevail.

Medical indications for cardiac replacement with either a mechanical device or organ transplant are sufficiently similar that the two approaches deal with overlapping patient populations. The development of a family of assist devices was based on a clinical strategy of providing short- to long-term assistance to a compromised ventricle, while the function of a total replacement device will be that of permanent and total cardiac replacement. Both assist devices and total replacement devices are already in use in several centers—and in a growing number of patients—as bridge devices, that is, to sustain candidates for cardiac transplant while awaiting the availability of a donor heart. It is inevitable that this application of mechanical cardiac devices will become more widespread and in the process will generate ethical dilemmas. Current medical criteria place the number of patients who might be accepted for cardiac transplant at a few thousand per year, but the number of donor hearts available for transplant has never reached 1,000 and is not likely to exceed 1,500 per year.[13] The use of an artificial heart device as a bridge cannot

increase the total number of transplants but will inevitably create ethical issues in patient selection.

The availability of an operationally successful, total artificial heart will have a substantial impact on our society: the number of possible candidates—17,000 to 35,000—speaks to the potential for societal benefit, but those numbers also introduce questions of how this scarce resource will be distributed and paid for. Health care in general is both a benefit and burden; the artificial heart is a special case in point. How much of society's resources should be allocated for health care? and, more specifically, how much of society's resources should be allocated to the artificial heart? Other questions involve how access is to be secured, which societal institution should deliver it and who should pay for it. Because the artificial heart has been developed from tax revenues, should not every citizen have the right to such, if needed? In fact, an earlier Congress declared that every citizen has the right to health care, but failed to provide either a definition or an appropriation. The questions of whether a person has a right to health and to health care and, if so, how much, were addressed in some detail by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.[14] A realistic question is whether the right to health care differs from other basic needs such as food and housing. A practical answer is that medical care is not distributed any more equitably than other goods and services of society.

To these questions one must add that of whether one has a right to an artificial heart. It has been stated that our concept of rights is a political one that evolved from the works of Locke, Rousseau and others, who proposed rights as spheres of activity in which persons might be free from interference. That is, rights were defined as the claim of an individual against deprivation as, for example, the Bill of Rights, which holds that no one may be deprived of life, liberty or the pursuit of happiness. It is only recently that this concept has been transformed into a positive claim on society as, for example, the right to work or the right to health. The transformation has been clumsy and awkward. Expensive and scarce medical resources, such as the artificial heart, tend to complicate the issues, for the right to something necessarily implies the duty to provide it, which in turn raises the issues of who shoulders this obligation and to what extent it should prevail over the provider's own well-being. This is further complicated by the fact that rights tend to be asserted as absolute—that is, they "trump" concerns such as practicality and convenience. Further, there are in fact limits to all rights. A commonly cited example is that of free speech—freedom of speech does not confer the right to shout "fire" in a crowded theater. One analogy of this to health care may well be that people have a right to be protected against polluted water and air, infectious diseases and to other common public health measures, but some will hold that this right might well not extend to provision of an artificial heart.

Immediately following their discovery or development, new medical therapies and technologies often tend to be in short supply—for instance, penicillin or renal dialysis. This inevitably creates societal dilemmas over the means of equitably distributing these scarce resources. In general, society has evolved three mechanisms for allocating scarce resources. The marketplace is the actual basis on which most resources, including medical care, are distributed today. Regardless of whether the resource be primary and simple—immunization, glasses, teeth—or tertiary—computed tomographic scan, coronary artery bypass grafting, cesarean section—there is an economic gradient to access. The marketplace is clearly the primary mechanism by which scarce resources, including medical care, are allocated by the current administration. In contrast, the utilitarian distribution scheme would allocate scarce resources to persons on the basis of their worth to society. This was the criterion used 20 years ago by a committee appointed to select the limited number of patients who could be treated during the early development of long-term renal dialysis. This approach would be rejected today. Finally, the egalitarian approach is effectively a lottery in which all candidates have equal opportunity and is the approach favored by ethicists and philosophers. The 1973 Artificial Heart Review Panel recommended that under the circumstances in which artificial heart resources are scarce, the selection of candidates should be on the basis of medical criteria; that if the patient pool exceeds the supply, selection should be by random process, and, specifically, that ability to pay should not be a criterion. These general principles have subsequently been affirmed by other review groups.

The propriety of expending large amounts of money to develop an artificial heart has come under serious questioning. Can or should society use its resources for this purpose? Is the artificial heart the best way to invest the large sums that will be required, and are there better alternatives? Could these resources better be invested in programs of immunization, prevention, nutrition, smoking education and so forth? These are not simple issues. Not all are willing to accept the argument that our resources are limited, nor that the nation's medical expenditures should be pegged at an arbitrary level, such as 10% of the gross national product. Others will hold that resources are finite and hence expenditures for an artificial heart will necessarily displace expenditures for public health measures, or medical research or even expenditures for the goods and services of society, such as food, welfare, national defense, alcohol abuse prevention and the like.

Summary

These complex issues cannot be resolved in the hour allocated for this conference. Some summary comment may be made, however. A starting point might be the question of whether development of the artificial heart should proceed. The facts are that it would be impossible to suppress further development—it is inevitable that fully implantable artificial hearts will continue to be developed. The intellectual resources are mobilized and committed, technology is at hand and the need and patient population have been identified. The technology is not proprietary within the United States; parallel programs have been under way in several countries and have reached advanced stages of development, notably in Japan and Germany. There is capital both here and abroad to manufacture the device. It remains only to specify whether one wishes a Buick or a Toyota.

A second question might be whether there will be patient demand. The data seem clear that a population will exist that could benefit. It seems extremely likely on the basis of recent experience with pacemakers, transplantation, coronary artery

bypass grafting, heart transplant and other procedures that the public and their physicians and surgeons will want and expect this device. The number is likely to be large enough to provide a market, and, in the manner of other new technologies, the medical indications for these devices are likely to expand. Experience also dictates that hospitals will compete for franchises.

There remains the question of resource allocation. The likelihood seems great that society will deal with this issue as it always has. Our current system of medical practice dictates that those people who want the device and can pay for it will probably get it, in much the same way they currently buy other medical goods and services. Our society, however, also has a strong ethic of rescue. It seems inevitable that availability of the device will become more nearly universal, and, whether by fees, premiums, taxes or special set-aside for entitlement, the costs will be paid by people.

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